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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/570,220	KASHMIRI ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *28-35 and 38-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27, 36-37 and 42-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/28/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The preliminary amendment filed 28 February 2006 has been entered in full.

Election/Restrictions

2. Applicant's election of the invention of Group I, claims 1-27, 36-37 and 42-43 in the reply filed on 12 May 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 28-35 and 38-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

4. Claims 1-27, 36-37 and 42-43 are under consideration.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 28 February 2008 have been fully considered by the examiner. A signed and initialed copy of the IDS is included with the instant Office Action.

Specification

6. The specification at pp. 20 and 31 discloses USSN 09/830,748, which is now issued and needs to be updated with the corresponding U.S. Patent number. USSN 09/830,748 is now U.S. Patent 6,818,749. Applicants' cooperation is requested in reviewing the entire disclosure for additional US Application serial numbers that require updating.

Appropriate correction is required.

Claim Objections

7. Claims 1, 9, 26 and 37 are objected to because of the following informalities:

a. Claims 1 and 37 are objected to in the recitation "humanized CC49 V10". It is suggested that the recitation "humanized CC49 V10" be amended to recite "huCC49V10" for consistency and readability of the claims.

b. Claim 9 is objected to in the recitation "sequence et forth s", which should read "sequence set forth as".

c. Claim 26 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form. Claim 26 recites wherein the antibody is encoded by a nucleic acid sequence as deposited as ATCC PTA-5415, which is disclosed in the specification as HuCC49V10 (e.g., see pg. 20), whereas the base claims recite humanized CC49 antibodies comprising additional human framework residues from the LEN light chain and from the 21/28' CL heavy chain relative to HuCC49V10. Thus, claim 26 is directed the HuCC49V10 antibody (ATCC PTA-5415) encoded by a nucleic acid as defined by the specification, and does not incorporate the LEN and 21/28' CL framework residues of the base claims. Accordingly, claim 26 does not incorporate every limitation of the base claim and add a limitation as required by the fourth paragraph of 35 U.S.C. 112. This paragraph states that "a claim in a dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers" and requires the dependent claim to further limit the subject matter claimed.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-27, 36-37 and 42-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-27, 36-37 and 42-43 are vague and indefinite in the recitation of "HuCC49V10" and "humanized CC49 V10" in claims 1 and 37 as the sole means of identifying the antibody. The use of laboratory designations to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. This rejection can be obviated by amending the claims to specifically and uniquely identify, for example, by SEQ ID number or by biological deposit accession number.

b. Claims 1-25, 27, 36 and 42-43 are indefinite in the recitation of amino acid positions in claims 1-7, 10-18 and 42-43. The claims recite particular amino acid residues or a subgenus of residues at a particular positions in the frameworks of the humanized anti-TAG-72 CC49 antibodies designated by position number, i.e., position 5, 19, 21 and 106. The claims do not define a reference sequence. The designation of particular amino acids at the recited positions is relative in nature because different sequences having different lengths and positions 5, 19, 21 and 106 may have different meanings. Further, antibodies may be numbered according to different numbering systems, i.e., Kabat or Chothia. As written, one of skill in the art would not be reasonably apprised of the metes and bounds of the claims. It is suggested that applicant amend the claims to include a reference sequence such that positions 5, 19, 21 and 106 of SEQ ID NO:X, for example, are definite.

c. Claims 10-19 are indefinite in the recitation "wherein the light chain framework comprises SEQ ID NO:X..." and "wherein the heavy chain framework comprises SEQ ID NO:Y…". Those of skill in the art recognize that the structure antibody light and heavy chains comprise three CDRs flanked by four framework regions, e.g., FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4 (e.g., see Figs. 3A and 4, Kashmiri et al, Methods, 36:25-34, 2005, IDS reference filed 2/28/06). Thus, it is unclear what is being referenced by the recitation "wherein the light chain framework comprises SEQ ID NO:X…" and "wherein the heavy chain framework comprises SEQ ID NO:Y…". Are the recited sequences

referencing individual framework regions, e.g., FR1, FR2, ect, and if so, which one, or do the phrases refer to the entire light chain frameworks and entire heavy chain frameworks or is some other meaning contemplated by the phrase?

d. Claim 26 is indefinite in the recitation "wherein the antibody is encoded by a nucleic acid sequence as deposited as ATCC-5415". The specification discloses that HuCC49V10 was deposited with the ATCC and assigned Accession No. PTA-5415 (see pg. 20). Thus, it appears that the claim is directed to the HuCC49V10 antibody (ATCC PTA-5415), which comprises a complete heavy chain and a complete light chain that associate via disulfide bonds and other non-covalent interactions, and which would not be encoded by a single nucleic acid, e.g., "encoded by a nucleic acid.." as presently recited. Thus, it is unclear (i) what the deposited biological material actually is, i.e., antibody HuCC49V10 or nucleic acids encoding such, and (ii) is the deposited antibody encoded by a single nucleic acid as presently recited, e.g., scFv, or is the antibody encoded by nucleic acids, e.g., one for the heavy chain and one for the light chain.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 1-27, 36-37 and 42-43 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is unclear if a cell line, which produces an antibody having the exact chemical identity of antibody huCC49V10 (ATCC accession no. PTA-5416) is known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit

of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Fundamental Immunology, William E. Paul, M.D. ed., 3rd ed., pg. 242, 1993. Therefore, it would require undue experimentation to reproduce the claimed antibody species antibody huCC49V10 deposited with the ATCC and assigned accession number PTA-5416.

The specification lacks complete deposit information for the deposit of anti-TAG-72 antibody huCC49V10. It is unclear whether antibodies possessing the identical properties of antibody huCC49V10 are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed antibody huCC49V10, a suitable deposit is required for patent purposes, evidence of public availability of the claimed antibody or evidence of the reproducibility without undue experimentation of the claimed antibody, is required.

Applicant's referral to the deposit of huCC49V10 as ATCC accession no. PTA-5416 on page 20 of the specification is an insufficient assurance that the required deposit has been made and all the conditions of 37 CFR 1.801-1.809 met.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit of antibody huCC49V10 has been

accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit of antibody huCC49V10 is not made under the provisions of the Budapest Treaty, then in order to certify that the deposit complies with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed. See MPEP 2406 and 37 CFR 1.804(b).

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

13. Claims 1-19 rejected under 35 U.S.C. 102(a) as being anticipated by Gonzales et al [a] (Proceedings of the American Association for Cancer Research, Annual meeting, vol. 44, pp. 1118, July 2003, IDS reference filed 2/28/06) as evidenced by Gonzales et al [b] (Molecular Immunology, 40(6):337-349, October 2003, IDS reference filed 2/28/06).

Gonzales et al [a] teaches a variant of the HuCC49V10 antibody, termed V59, in which murine VL framework residues 5, 19, 21, 43, 78, 100 and 106 of huCC49V10 were replaced with the corresponding residues of the human antibody LEN and murine VH framework residues 12, 20, 38, 40, 48, 66, 67, 69 and 80 of huCC49V10 were replaced with the corresponding residues of the human antibody 21/28'CL as evidenced by Gonzales et al [b]. Applicant is reminded that products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical

structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada* 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Thus, the V59 variant of HuCC49V10 of Gonzalez et al [a] necessarily comprises the framework and CDR sequences as presently recited.

Thus, Gonzalez et al [a] anticipate the claims as evidenced by Gonzales et al [b].

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1-25, 27 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gonzales et al [a] (Proceedings of the American Association for Cancer Research, Annual meeting, vol. 44, pp. 1118, July 2003, IDS reference filed 2/28/06) as evidenced by Gonzales et al [b] (Molecular Immunology, 40(6):337-349, October 2003, IDS reference filed 2/28/06) in view of Kashmiri et al (WO 00/26394, published 5/11/2000, IDS reference filed 2/28/06).

Gonzales et al [a] teach a variant of the HuCC49V10 antibody, termed variant 59 (V59), in which murine VL framework residues 5, 19, 21, 43, 78, 100 and 106 of huCC49V10 were replaced with the corresponding residues of the human antibody LEN and murine VH framework residues 12, 20, 38, 40, 48, 66, 67, 69 and 80 of huCC49V10 were replaced with the corresponding residues of the human antibody 21/28'CL as evidenced by Gonzales et al [b] and variant 59 is minimally immunogenic because of its low sera reactivity and is a potentially useful clinical reagent against human carcinomas according to Gonzales et al [a]. Gonzales et al [a] do not specifically teach wherein the antibody is a Fv, Fab, or a F(ab')2 fragment, or comprises a detectable label including a fluorescent or a radioactive molecule, or comprises an effector molecule including a toxin, or a pharmaceutical composition comprising the antibody and a pharmaceutically acceptable carrier, or a kit comprising a container comprising the antibody and instructions. These deficiencies are made up for in the teachings of Kashmiri et al.

Kashmiri et al teach humanized CC49 antibodies and antigen-binding fragments thereof (e.g., Fv, Fab, Fab', F(ab')2) and the humanized CC49 antibodies may be conjugated to various diagnostic or therapeutic agents (e.g., a radionuclide, fluor, enzyme, chemotherapeutic agent, ect) as well as pharmaceutical compositions comprising the humanized CC49 antibodies and a pharmaceutically acceptable carrier as well as a kit comprising the humanized CC49 antibodies and instructions for therapeutic benefit in human cancer patients (see entire document, particularly pp. 7-8, 17-18 and examples).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced humanized CC49 antibody variant 59 and antigen-binding fragments thereof (e.g., Fv, Fab, Fab', F(ab')2) linked to

a diagnostic or therapeutic agent (e.g., a radionuclide, fluor, enzyme, chemotherapeutic agent, ect) and kits and pharmaceutical compositions comprising such and a pharmaceutically acceptable carrier for therapeutic benefit in human carcinoma patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced humanized CC49 antibody variant 59 and antigen-binding fragments thereof (e.g., Fv, Fab, Fab', F(ab')2) linked to a diagnostic or therapeutic agent (e.g., a radionuclide, fluor, enzyme, chemotherapeutic agent, ect) and kits and pharmaceutical compositions comprising such and a pharmaceutically acceptable carrier for therapeutic benefit in human carcinoma patients in view of Gonzales et al [a] as evidenced by Gonzales et al [b] and Kashmiri et al because Gonzales et al [a] teach a variant of the HuCC49V10 antibody, termed variant 59 (V59), in which murine VL framework residues 5, 19, 21, 43, 78, 100 and 106 of huCC49V10 were replaced with the corresponding residues of the human antibody LEN and murine VH framework residues 12, 20, 38, 40, 48, 66, 67, 69 and 80 of huCC49V10 were replaced with the corresponding residues of the human antibody 21/28'CL as evidenced by Gonzales et al [b] and variant 59 is minimally immunogenic because of its low sera reactivity and is a potentially useful clinical reagent against human carcinomas according to Gonzales et al [a] and Kashmiri et al teach humanized CC49 antibodies and antigen-binding fragments thereof (e.g., Fv, Fab, Fab', F(ab')2) and the humanized CC49 antibodies may be conjugated to various diagnostic or therapeutic agents (e.g., a radionuclide, fluor, enzyme, chemotherapeutic agent, ect) as well as pharmaceutical compositions comprising the humanized CC49 antibodies and a pharmaceutically acceptable carrier as well as a kit comprising the humanized CC49 antibodies and instructions for therapeutic benefit in human cancer patients. Therefore, one of ordinary skill in the art would have been motivated at the time the invention was made to produce variant 59 and antigen-binding fragments thereof (e.g., Fv, Fab, Fab', F(ab')2) linked to a diagnostic or therapeutic agent (e.g., a radionuclide, fluor, enzyme, chemotherapeutic agent, ect) and kits and pharmaceutical compositions comprising such and a pharmaceutically acceptable carrier for therapeutic

benefit in human carcinoma patients, since variant 59 is minimally immunogenic because of its low sera reactivity and is a potentially useful clinical reagent against human carcinomas according to Gonzales et al [a]. Thus, it would have been *prima facie* obvious to one skilled in the art to have produced humanized CC49 antibody variant 59 and antigen-binding fragments thereof (e.g., Fv, Fab, Fab', F(ab')2) linked to a diagnostic or therapeutic agent (e.g., a radionuclide, fluor, enzyme, chemotherapeutic agent, ect) and kits and pharmaceutical compositions comprising such and a pharmaceutically acceptable carrier for therapeutic benefit in human carcinoma patients in view of Gonzales et al [a] as evidenced by Gonzales et al [b] and Kashmiri et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

16. Claims 1 and 42-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gonzales et al [a] (Proceedings of the American Association for Cancer Research, Annual meeting, vol. 44, pp. 1118, July 2003, IDS reference filed 2/28/06) as evidenced by Gonzales et al [b] (Molecular Immunology, 40(6):337-349, October 2003, IDS reference filed 2/28/06) in view of Gonzales et al [c] (Proceedings of the American Association for Cancer Research, Annual meeting, vol. 44, pp. 1116, July 2003, IDS reference filed 2/28/06) as evidenced by Pascalis et al (Clinical Cancer research, 9:5521-5531, November 2003, IDS reference filed 2/28/06).

Gonzales et al [a] as evidenced by Gonzales et al [b] have been described supra. Gonzalez et al [a] does not teach wherein the antibody further comprises a tyrosine to proline substitution in L-CDR3 at position 91 and a valine to leucine substitution at position 27b. Theses deficiencies are made up for in the teachings of Gonzalez et al [c] as evidenced by Pascalis et al.

Gonzalez et al [c] teach humanized CC49 antibody variants of HuCC49V10, wherein two variants V14 and V15 have a higher binding affinity and much lower sera reactivity than the parental huCC49V10 antibody and are potentially excellent reagents for clinical applications (see entire document). As evidenced by Pascalis et al,

huCC49V10 variant V14 comprises a tyrosine to proline substitution at Kabat position 91 in L-CDR3 and variant 15 comprises the tyrosine to proline substitution at Kabat position 91 in L-CDR3 and a valine to leucine substitution at Kabat position 27b in L-CDR1 (see Fig. 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced humanized CC49 antibody variant 59 further comprising a tyrosine to proline substitution in at Kabat position 91 in L-CDR3 and a valine to leucine substitution at Kabat position 27b in L-CDR1 for therapeutic benefit in human carcinoma patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced humanized CC49 antibody variant 59 further comprising a tyrosine to proline substitution in L-CDR3 at position 91 and a valine to leucine substitution at position 27b in L-CDR1 for therapeutic benefit in human carcinoma patients in view of Gonzales et al [a] as evidenced by Gonzales et al [b] and Gonzalez et al [c] as evidenced by Pascalis et al because Gonzales et al [a] teach a variant of the HuCC49V10 antibody, termed variant 59 (V59), in which murine VL framework residues 5, 19, 21, 43, 78, 100 and 106 of huCC49V10 were replaced with the corresponding residues of the human antibody LEN and murine VH framework residues 12, 20, 38, 40, 48, 66, 67, 69 and 80 of huCC49V10 were replaced with the corresponding residues of the human antibody 21/28'CL as evidenced by Gonzales et al [b] and variant 59 is minimally immunogenic because of its low sera reactivity and is a potentially useful clinical reagent against human carcinomas according to Gonzales et al [a] and Gonzalez et al [c] teach humanized CC49 antibody variants of HuCC49V10, wherein two variants V14 and V15 have a higher binding affinity and much lower sera reactivity than the parental huCC49V10 antibody and are potentially excellent reagents for clinical applications, wherein V14 necessarily comprises a tyrosine to proline substitution at Kabat position 91 in L-CDR3 and V15 comprises the tyrosine to proline substitution in at Kabat position 91 in L-CDR3 and a valine to leucine substitution at Kabat position 27b in L-CDR1 as evidenced by Pascalis et al. Therefore, at the time the invention was made one of

ordinary skill in the art would have been motivated to incorporate the amino acid substitutions of HuCC49V10 variants V14 and V15 (i.e., tyrosine to proline substitution in at Kabat position 91 in L-CDR3 and a valine to leucine substitution at Kabat position 27b in L-CDR1) into the HuCC49V10 variant 59 of Gonzalez et al [a] in order to produce a huCC49V10 variant having higher binding affinity and much lower sera reactivity compared to HuCC49V10 for clinical applications in human carcinoma patients. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Thus, it would have been *prima facie* obvious to one skilled in the art to have produced humanized CC49 antibody variant 59 further comprising a tyrosine to proline substitution in L-CDR3 at position 91 and a valine to leucine substitution at position 27b in L-CDR1 for therapeutic benefit in human carcinoma patients in view of Gonzales et al [a] as evidenced by Gonzales et al [b] and Gonzalez et al [c] as evidenced by Pascalis et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-22, 24-27 and 36-37 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-47 of U.S. Patent No. 6,818,749 in view of Gonzales et al [a] (Proceedings of the American Association for Cancer Research, Annual meeting, vol. 44, pp. 1118, July 2003, IDS reference filed 2/28/06) as evidenced by Gonzales et al [b] (Molecular Immunology, 40(6):337-349, October 2003, IDS reference filed 2/28/06).

Claims 1-47 of U.S. Patent No. 6,818,749 are drawn to humanized anti-TAG-72 CC49 antibody, HuCC49V10 and antigen-binding fragments thereof including an Fv, a Fab and a F(ab')2, wherein the HuCC49V10 carries the L-CDR-1 and L-CDR2 of the human antibody LEN, and a threonine at position 97 in the CC49 L-CDR3 is replaced with a serine residue present at the corresponding position in the human antibody LEN and the variant HuCC49V10 also comprises an asparagine at position 60 in the murine CC49 H-CDR2 is replaced with a serine, a glutamic acid at position 61 in the murine CC49 H-CDR2 is replaced with a glutamine, an arginine at position 62 in the murine CC49 H-CDR2 is replaced with a lysine, and a lysine at position 64 in the murine CC49 H-CDR2 is replaced with a glutamine, wherein the HuCC49V10 is radiolabeled and compositions comprising the HuCC49V10 and a pharmaceutically acceptable carrier as well as a kit comprising said antibody. Claims 1-47 do not specifically teach wherein the HuCC49V10 further comprises murine VL framework residues 5, 19, 21, 43, 78, 100 and 106 of huCC49V10 were replaced with the corresponding residues of the human antibody LEN and murine VH framework residues 12, 20, 38, 40, 48, 66, 67, 69 and 80

of huCC49V10 were replaced with the corresponding residues of the human antibody 21/28'CL. These deficiencies are made up for in the teachings of Gonzales et al [a] as evidenced by Gonzales et al [b].

Gonzales et al [a] as evidenced by Gonzales et al [b] has been described supra.

The claims in the instant application are obvious variants of claims 1-47 of U.S. Patent No. 6,818,749 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced humanized CC49 antibody variant 59 and antigen-binding fragments thereof (e.g., Fv, Fab, Fab', F(ab')2) linked to a diagnostic or therapeutic agent (e.g., a radionuclide) and kits and pharmaceutical compositions comprising variant 59 and a pharmaceutically acceptable carrier for therapeutic benefit in human carcinoma patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced humanized CC49 antibody variant 59 and antigen-binding fragments thereof (e.g., Fv, Fab, Fab', F(ab')2) linked to a diagnostic or therapeutic agent (e.g., a radionuclide) and kits and pharmaceutical compositions comprising variant 59 and a pharmaceutically acceptable carrier for therapeutic benefit in human carcinoma patients in view of claims 1-47 of U.S. Patent No. 6,818,749 and Gonzales et al [a] as evidenced by Gonzales et al [b] because Gonzales et al [a] teach a variant of the HuCC49V10 antibody, termed variant 59 (V59), in which murine VL framework residues 5, 19, 21, 43, 78, 100 and 106 of huCC49V10 were replaced with the corresponding residues of the human antibody LEN and murine VH framework residues 12, 20, 38, 40, 48, 66, 67, 69 and 80 of huCC49V10 were replaced with the corresponding residues of the human antibody 21/28'CL as evidenced by Gonzales et al [b] and variant 59 is minimally immunogenic because of its low sera reactivity and is a potentially useful clinical reagent against human carcinomas according to Gonzales et al [a]. Therefore, one of ordinary skill in the art would have been motivated to produce variant 59 and antigen-binding fragments thereof (e.g., Fv, Fab, Fab', F(ab')2) linked to a diagnostic or therapeutic agent (e.g., a radionuclide, fluor,

enzyme, chemotherapeutic agent, ect) and kits and pharmaceutical compositions comprising such and a pharmaceutically acceptable carrier for therapeutic benefit in human carcinoma patients, since variant 59 is minimally immunogenic because of its low sera reactivity and is a potentially useful clinical reagent against human carcinomas according to Gonzales et al [a]. Thus, it would have been *prima facie* obvious to have produced humanized CC49 antibody variant 59 and antigen-binding fragments thereof (e.g., Fv, Fab, Fab', F(ab')2) linked to a diagnostic or therapeutic agent (e.g., a radionuclide) and kits and pharmaceutical compositions comprising variant 59 and a pharmaceutically acceptable carrier for therapeutic benefit in human carcinoma patients in view of claims 1-47 of U.S. Patent No. 6,818,749 and Gonzales et al [a] as evidenced by Gonzales et al [b].

19. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

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